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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/704,306	11/02/2000	James P. Beck	PH-7032	4919

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ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 10/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/704,306	BECK et al.
Examiner	**Art Unit**
Brenda Coleman	1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov. 7, 2002, June 12, 2003 and July 19, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-12, 14-28, and 30-92* is/are pending in the application.

4a) Of the above, claim(s) *37-41 and 48* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-12, 14-28, 30-36, 42-47, and 49-92* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *14 & 16*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-12, 14-28 and 30-92 are pending in the application.

This action is in response to applicants' amendments filed November 7, 2002, June 12, 2003 and July 19, 2003. Claims 1, 14 and 30-32 have been amended and claim 50 is newly added by the amendment of November 7, 2002. Claims 51-92 are newly added by the amendment of June 12, 2003. Claims 31, 32, 80 and 81 have been amended by the amendment of July 19, 2003.

Response to Amendment

Applicant's amendments filed November 7, 2002, June 12, 2003 and July 19, 2003 have been fully considered with the following effect:

Election/Restriction

1. It is acknowledged that the Applicant's have affirmed their election of Group I in Paper No. 19. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 37-41 and 48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 19.

3. The applicants' amendments are sufficient to overcome the 35 U.S.C. § 112, second paragraph rejections of the last office action, which are hereby **withdrawn**.

4. The applicants' amendments are sufficient to overcome the 35 U.S.C. § 112, first paragraph rejections of the last office action, which are hereby **withdrawn**.

5. With regards to the 35 U.S.C. § 102 anticipation rejection of claims 1-36, 43-47 and 49 of the last office action, the applicant's amendments and arguments have been fully considered but are not found persuasive. The applicants stated that "the accompanying Declaration of Bruce F. Molino under 37 C.F.R.§ 1.132 ("Molino Declaration") is presented to demonstrate that compounds of the present application achieve a binding affinity for DAT to binding affinity for NET ratio of at least 2:1 and a binding affinity for SERT to binding affinity for NET ration of at least 20:1, while dichlofensine and a metabolite of dichlofensine do not (Molino Declaration ¶4)". However, as stated below in the rejections under 35 U.S.C. 112, first and second paragraphs the binding affinity ratios claimed herein are vague and indefinite in that it is not known if these ratios are the same in different medias or conditions as those presented in the declaration, nor is there support for the ratios or multiple assays to effectively discard dichlofensine from the compounds of the instant invention. Rheiner, CH 538 477, DE 2 062 001 and U.S. equivalent 3,947,456 are silent to the mode of action of the compounds of formula I, but possess a common utility.

Claims 1-12, 14-28, 30-36, 42-47 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Tirelli et al., The Journal of Pharmacology and Experimental Therapeutics. For reasons of record and stated above.

6. Claims 1-12, 14-28, 30-36, 42-47 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Salama et al., British Journal of Haematology. For reasons of record and stated above.

7. Claims 1-12, 14-28, 30-36, 42-47 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Dr. Alfred Rheiner, CH 538 477 (U.S. equivalent 3,947,456). For reasons of record and stated above.

8. Claims 1-12, 14-28, 30-36, 42-47 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Dr. Alfred Rheiner, DE 2 062 001 (U.S. equivalent 3,947,456). For reasons of record and stated above.

9. With regards to the 35 U.S.C. § 103 obviousness rejection of claims 1-36, 43-47 and 49 of the last office action, the applicant's amendments and arguments have been fully considered but are not found persuasive. The applicants stated that "the Molino Declaration demonstrated that dichlofensine and the above-described metabolite of dichlofensine, which are preferred by the German Application do not meet the claimed selectivity". However, as stated above in response to the 102 rejection, the binding affinity ratios claimed herein are vague and indefinite in that it is

not known if these ratios are the same in different medias or conditions as those presented in the declaration, nor is there support for the ratios or multiple assays to effectively discard dichlofensine from the compounds of the instant invention. Rheiner, CH 538 477, DE 2 062 001 and U.S. equivalent 3,947,456 are silent to the mode of action of the compounds of formula I, but possess a common utility.

Claims 1-12, 14-28, 30-36, 42-47 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dr. Alfred Rheiner, CH 538 477 (U.S. equivalent 3,947,456). For reasons of record and stated above.

10. Claims 1-12, 14-28, 30-36, 42-47 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dr. Alfred Rheiner, DE 2 062 001 (U.S. equivalent 3,947,456). For reasons of record and stated above.

11. The applicants' amendments are sufficient to overcome the 35 U.S.C. § 103 obviousness rejection of claims 1-36, 43-47 and 49 as being unpatentable over JP 4193867, in the last office action, which is hereby **withdrawn**.

12. The applicants' amendments are sufficient to overcome the 35 U.S.C. § 103 obviousness rejection of claims 30, 33 and 34 as being unpatentable over Trepanier et al., Journal of Medicinal Chemistry, in the last office action, which is hereby **withdrawn**.

13. The applicants' amendments are sufficient to overcome the 35 U.S.C. § 103 obviousness rejection of claims 30, 33 and 34 as being unpatentable over Modeshka et al., CA 2015114, in the last office action, which is hereby **withdrawn**.

14. The applicants' amendments are sufficient to overcome the 35 U.S.C. § 103 obviousness rejection of claims 30, 33 and 34 as being unpatentable over Miller et al., Synthetic Communications, in the last office action, which is hereby **withdrawn**.

15. With regards to the 35 U.S.C. § 103 obviousness rejection of claims 30, 33 and 34 of the last office action, the applicant's amendments and arguments have been fully considered but are not found persuasive. The applicants stated that "the reference does not suggest the claimed DAT/NET ration of at least 2:1 and SERT/NET ratio of at least about 20:1". However, as stated above in response to the 102 rejection, the binding affinity ratios claimed herein are vague and indefinite in that it is not known if these ratios are the same in different medias or conditions as those presented in the declaration, nor is there support for the ratios or multiple assays to effectively discard the properties of the Tirelli compounds from the compounds of the instant invention.

Claims 30, 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tirelli et al. For reasons of record and stated above.

In view of the amendment dated November 7, 2002, June 12, 2003 and July 19, 2003, the following new grounds of rejection and/or reinstated rejections apply:

Information Disclosure Statement

16. The information disclosure statement filed August 29, 2001 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Two of the references were not available to the current examiner of record and the 1449 is incomplete. It is therefore requested that these references and/or their dates of publication be provided so that the 1449 can be completed. The two reference are JORGENSON, Preparation of Ketones from the Reaction of Organolithium Reagents with Carboxylic Acids and BLOMBERG et al. The Barbier Reaction - A One Step Alternative for Syntheses via Organomagnesium Compounds.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 1-12, 14-28, 30-36, 42-47 and 49-92 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way

as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amendment of claim 1 and the addition of claim 51, includes a limitation at the end of each of the independent claims, which is not described in the specification, i.e. wherein the compound has a binding affinity for dopamine transporter protein to a binding affinity for norepinephrine transporter protein ratio of at least 2:1 and a binding affinity for serotonin transporter protein to a binding affinity for norepinephrine transporter protein ratio of at least 20:1.

Applicant is required to cancel the new matter in the reply to this Office action.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 1-12, 14-28, 30-36, 42-47 and 49-92 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a) Claims 1-12, 14-28, 30-36, 42-47 and 49-92 are vague and indefinite in that it is not known what is meant by added limitation "wherein the compound has a binding affinity for dopamine transporter protein to a binding affinity for norepinephrine transporter protein ratio of at least 2:1 and a binding affinity for serotonin transporter protein to a binding affinity for norepinephrine transporter protein ratio of at least 20:1". Too much depends on perception by the reader

since there are an assortment of possible environments in which to measure *in vitro*, *in vivo* (mice, rats, nonmurine hosts) along with different types of testing such that one cannot readily determine which compounds are within the instant scope. There are many different assays for testing binding affinity as exemplified by the applicants.

b) Claims 1, 51 (and claims dependent thereon) are vague and indefinite in that it is not known what is meant by the moiety C_1-C_4 halolkyl in the definition of R^4.

c) Claims 1, 51 (and claims dependent thereon) are vague and indefinite in that it is not known what is meant by the definition of R^5 **or** R^6 are **each independently** - O-C(R^{12})$_2$-O- in compounds of the formulae IE.

d) Claims 1, 51 (and claims dependent thereon) are vague and indefinite in that it is not known what is meant by the definition of R^7 and R^6 can **independently** also be -O-C(R^{12})$_2$-O- in compounds of the formulae IE.

e) Claims 1, 51 (and claims dependent thereon) are vague and indefinite in that it is not known what is meant by the proviso where only one of R^9 and R^{10} **or** R^9 and R^{10} are taken together with the nitrogen....

f) Claims 23, 73 (and claims dependent thereon) are vague and indefinite in that it is not known what is meant by the definition of R^4 where each of which is optionally substituted with from 1 to 3 substitutents. It is not known how H can be substituted.

g) Claims 24 and 74 are vague and indefinite in that it is not known what is meant by the defiinition of R^4 where R^4 is F methyl.

h) Claim 30 recites the limitation "7-fluoro-4-(4-methoxy)phenyl-2-methyl-1,2,3,4-tetrahydroisoquinoline" in the 16th species. There is insufficient antecedent basis for this limitation in the claim.

i) Claim 30 recites the limitation "7-cyano-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline" in the 22nd species. There is insufficient antecedent basis for this limitation in the claim.

j) Claim 30 recites the limitation "2-methyl-4-phenyl-7-trifluoromethoxy-1,2,3,4-tetrahydroisoquinoline" in the 30th species. There is insufficient antecedent basis for this limitation in the claim.

k) Claim 30 recites the limitation "8-methoxy-2-methyl-4-(4-methyl)phenyl-1,2,3,4-tetrahydroisoquinoline" in the 61st species. There is insufficient antecedent basis for this limitation in the claim.

l) Claim 30 is vague and indefinite in that it is not known what is meant by the 69th species which is missing a close parenthesis in the nomenclature.

m) Claim 30 is vague and indefinite in that it is not known what is meant by the 71st species which is missing an open parenthesis in the nomenclature.

n) Claim 30 is vague and indefinite in that it is not known what is meant by N-methyl(2-methyl-4-phenyl-1,2,3,4-tetrahydro-7-isoquinolinyl)-N-

methylmethanamine (72nd species) of which it appears that the amine nitrogen is substituted 4 times.

o) Claim 30 recites the limitation "8-hydroxy-2-methyl-4-phenyl-1,2,3,4-tetrahydro-7-isoquinolinecarbonitrile" in the 73rd species. There is insufficient antecedent basis for this limitation in the claim.

p) Claim 31 recites the limitation "Me, H, H, F, H, OMe, H, H" in the definition of R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8, respectively, in the 11th species on page 2 of the amendment filed July 29, 2003. There is insufficient antecedent basis for this limitation in the claim.

q) Claim 31 recites the limitation "Me, H, H, CN, H, H, H, H" in the definition of R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8, respectively, in the 17th species on page 2 of the amendment filed July 29, 2003. There is insufficient antecedent basis for this limitation in the claim.

r) Claim 31 recites the limitation "Me, H, H, OCF_3, H, H, H, H" in the definition of R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8, respectively, in the 25th species on page 2 of the amendment filed July 29, 2003. There is insufficient antecedent basis for this limitation in the claim.

s) Claim 31 is vague and indefinite in that it is not known what is meant by O(4-OmePh) in the definiton of R^4 of the 17th species from the bottom of page 2 of the amendment filed July 29, 2003.

t) Claim 31 recites the limitation "Me, H, OMe, H, H, Me, H, H" in the definition of R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8, respectively, in the 9th species on page 3 of the amendment filed July 29, 2003. There is insufficient antecedent basis for this limitation in the claim.

u) Claim 31 recites the limitation "Me, H, OH, CN, H, H, H, H" in the definition of R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8, respectively, in the 23rd species on page 3 of the amendment filed July 29, 2003. There is insufficient antecedent basis for this limitation in the claim.

v) Claim 32 recites the limitation "H, H, Me, F" in the definition of R^1, R^2, R^3 and R^4, respectively, in the 1st species on page 3 of the amendment filed July 29, 2003. There is insufficient antecedent basis for this limitation in the claim.

w) Claim 32 recites the limitation "OMe, H, F, F" in the definition of R^1, R^2, R^3 and R^4, respectively, in the 2nd species on page 3 of the amendment filed July 29, 2003. There is insufficient antecedent basis for this limitation in the claim.

x) Claim 32 recites the limitation "H, H, Cl, F" in the definition of R^1, R^2, R^3 and R^4, respectively, in the 4th species on page 3 of the amendment filed July 29, 2003. There is insufficient antecedent basis for this limitation in the claim.

y) Claim 32 recites the limitation "H, H, F, F" in the definition of R^1, R^2, R^3 and R^4, respectively, in the 5th species on page 3 of the amendment filed July 29, 2003. There is insufficient antecedent basis for this limitation in the claim.

z) Claim 32 recites the limitation "Me, F, H, F" in the definition of R^1, R^2, R^3 and R^4, respectively, in the 6th species on page 3 of the amendment filed July 29, 2003. There is insufficient antecedent basis for this limitation in the claim.

aa) Claims 36, 43-45, 85 and 87-89 are vague and indefinite in that the claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining which are the disorders created by or is dependent upon decreased availability of serotonin, norepinephrine or dopamine or inhibiting synaptic norepinephrine uptake, serotonin uptake or dopamine uptake. Determining whether a given disease responds or does not respond to such an inhibitor will involve undue experimentation. Suppose that a given drug, which has inhibitor properties *in vitro*, when administered to a patient with a certain disease, does not produce a favorable response. One can not conclude that specific disease does not fall within this claim. Keep in mind that:

A. It may be that the next patient will respond. No pharmaceutical has 100% efficacy. What success rate is required to conclude our drug is a treatment? Thus, how many patients need to be treated? If "successful treatment" is what is intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in 100? 1,000? 10,000? Will the standard vary depending on the current therapy for the disease?

B. It may be that the wrong dosage or dosage regimen was employed. Drugs with similar chemical structures can have markedly different pharmacokinetics and metabolic fates. It is quite common for pharmaceuticals to work and or be safe at one dosage, but not at another that is significantly higher or lower. Furthermore, the dosage regimen may be vital --- should the drug be given e.g. once a day, or four times in divided dosages? The optimum route of administration can not be predicted in advance. Should our drug be given as a bolus *iv* or in a time release *po* formulation. Thus, how many dosages and dosage regimens must be tried before one is certain that our drug is not a treatment for this specific disease?

C. It may be that our specific drug, while active *in vitro*, simply is not potent enough or produces such low concentrations in the blood that it is not an effective treatment of the specific disease. Perhaps a structurally related drug is potent enough or produces high enough blood concentrations to treat the disease in question, so that the first drug really does fall within the claim. Thus, how many different structurally related inhibitors must be tried before one concludes that a specific compound does not fall within the claim?

D. Conversely, if the disease responds to our second drug but not to the first, both of whom are inhibitors *in vitro*, can one really conclude that the disease falls within the claim? It may be that the first compound result is giving the

accurate answer, and that the success of second compound arises from some other unknown property which the second drug is capable. It is common for a drug, particularly in attention deficit hyperactivity disorder, to work by many mechanisms. The history of psychopharmacology is filled with drugs, which were claimed to be a pure receptor XYX agonist or antagonist, but upon further experimentation shown to effect a variety of biological targets. In fact, the development of a drug for a specific disease and the determination of its biological site of action usually precede linking that site of action with the disease. Thus, when mixed results are obtained, how many more drugs need be tested?

E. Suppose that our drug is an effective treatment of the disease of interest, but only when combined with some totally different drug. There are for example, agents in antiviral and anticancer chemotherapy which are not themselves effective, but are effective treatments when the agents are combined with something else.

Consequently, determining the true scope of the claim will involve extensive and potentially inconclusive research. Without it, one skilled in the art cannot determine the actual scope of the claim. Hence, the claim is indefinite.

ab) Regarding claim 42, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

ac) Claim 73 is vague and indefinite in that it is not known what is meant by the definition of R^5, R^6 and R^7 where R^5, R^6 and R^7 is optionally C_1-C_6 alkyl.

ad) Claim 79 recites the limitation "7-fluoro-4-(4-methoxy)phenyl-2-methyl-1,2,3,4-tetrahydroisoquinoline" in the 16th species. There is insufficient antecedent basis for this limitation in the claim.

ae) Claim 79 recites the limitation "7-cyano-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline" in the 22nd species. There is insufficient antecedent basis for this limitation in the claim.

af) Claim 79 is vague and indefinite in that it is not known what is meant by the 69th species which is missing a close parenthesis in the nomenclature.

ag) Claim 79 is vague and indefinite in that it is not known what is meant by the 71st species which is missing an open parenthesis in the nomenclature.

ah) Claim 79 is vague and indefinite in that it is not known what is meant by N-methyl(2-methyl-4-phenyl-1,2,3,4-tetrahydro-7-isoquinolinyl)-N-methylmethanamine (72nd species) of which it appears that the amine nitrogen is substituted 4 times.

ai) Claim 80 recites the limitation "Me, H, H, F, H, OMe, H, H" in the definition of R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8, respectively, in the 15th species on page 4 of the amendment filed July 29, 2003. There is insufficient antecedent basis for this limitation in the claim.

aj) Claim 80 recites the limitation "Me, H, H, CN, H, H, H, H" in the definition of R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8, respectively, in the 21st species on page 4 of the amendment filed July 29, 2003. There is insufficient antecedent basis for this limitation in the claim.

ak) Claim 80 is vague and indefinite in that it is not known what is meant by O(4-OmePh) in the definiton of R^4 of the last species on the bottom of page 4 of the amendment filed July 29, 2003.

al) Claim 81 recites the limitation "Me, F, H, F" in the definition of R^1, R^2, R^3 and R^4, respectively, in the 2nd species on page 6 of the amendment filed July 29, 2003. There is insufficient antecedent basis for this limitation in the claim.

am) Regarding claim 86, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. Claims 1-5, 10, 16, 28, 35, 36, 42, 45, 51-55, 84-86 and 89 are rejected under 35 U.S.C. 102(b) as being anticipated by Brenner et al., U.S. 4,340,600. Brenner teaches the compounds of the instant invention where R^1 is methyl, R^2 is hydrogen, R^3 is SMe or OAc, R^4 is hydrogen, R^5 is OH, OAc or OMe, R^6 is OH, OAc or OMe, R^7 is hydrogen and R^8 is hydrogen. See examples 9 and 10.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is (703) 305-1880. The examiner can normally be reached on Mondays from 8:30 AM to 5:00 PM, on Tuesdays from 8:00 AM to 4:30 PM, on Wednesday thru Friday from 9:00 AM to 5:30 PM.

The fax phone number for this Group is (703) 308-4734 for "unofficial" purposes and the actual number for **OFFICIAL** business is **308-4556**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brenda Coleman

Brenda Coleman
Primary Examiner AU 1624
October 20, 2003